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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
GORDON, BRIAN R

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,356	YAO ET AL.	
	Examiner	Art Unit	
	Brian R. Gordon	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40 and 62-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40 and 62-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-10-02, 12-10-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group III in the reply filed on January 28, 2005 is acknowledged.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Interpretation

3. The examiner interprets the structure of claim 40 as being a pin tool comprising one or more slotted pins each having an open tip. As to the "adapted to" clauses:

It has been held that the recitation that an element is "adapted to" or "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites wherein the first material **is or is** dimethyldichlorosilane

(DMDCS). The claim incorporates "or is" as to imply there is an alternative present. However there is only one material listed as such the "or is" should be deleted.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 40 and 62-65 rejected under 35 U.S.C. 102(e) as being anticipated by Martinsky US 6,101,946.

Martinsky discloses a device for fabricating microarrays of biochemical substances, consisting of a holder and one or more printing pins. The holder contains apertures with regular spacing that define the location of one or more printing pins during the printing process. The tip of each printing pin contains a sample channel that holds a predetermined volume of biological or chemical sample (abstract).

The EDM is then used to cut the sample channel 22 to a depth 202. Thus, as illustrated in FIG. 2A, the sample channel is cut from one side of point 20 to the other and is, consequently, an exterior sample channel. The sample channel may have a depth, for example, may be 0.125" (3,175 μm – claim 64) and a width 200 of 0.004" +- 0.002" (101.6 μm – claim 62). The width of the wire and the extent of bending

(described below) determines the volume of the sample channel 22. For example, a 4 mil (0.004") EDM wire that makes a cut 0.125" deep into the pin shaft 28 provides a sample channel 22 with a volume of 0.2 μl after bending. Larger wires and different cutting routines can be used to prepare custom sample channels such as those with an expanded sample reservoir as depicted in FIG. 4 (column 4, lines 46-67).

As to claim 65, as seen in the figures the tips of the pins are tapered.

8. Claim 40, 65, and 81 are rejected under 35 U.S.C. 102(a) as being anticipated by Moore et al. WO 00/25923.

Moore et al. discloses a dropping tool for transferring drops of a liquid onto a substrate wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region. A dropping tool for transferring drops of liquid onto a substrate, the dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool. A method for transferring drops of liquid carried on a dropping tool onto a substrate to form an ordered array of drops thereon wherein the drop of liquid is transferred without contacting the dropping

tool with the substrate either directly or indirectly via the drop of liquid (abstract, see also figures). As seen in figure 8, the tip is tapered.

FIG. 1 shows a cross-sectional view of the lower section of a dropping tool according to a first embodiment of the present invention for transferring drops of an aqueous liquid onto a solid substrate. In this embodiment the dropping tool is a steel pin substrate 12 having its whole surface other than a region at its tip 14 coated with a layer 16 of a relatively hydrophobic material such as teflon or tetrahedral amorphous carbon (t.a.c).

9. Claim 40 is rejected under 35 U.S.C. 102(e) as being anticipated by Feygin US 6,116,297.

Feygin discloses dispenser suitable for dispensing a small volume of liquid. The liquid dispenser has a capillary channel suitable for aspirating and retaining a predetermined and repeatable volume of liquid via capillary action. To dispense retained liquid, the capillary channel is accelerated and then abruptly decelerated. Liquid is supplied to the capillary channel via a liquid-supply conduit that is in fluid communication therewith. When the capillary channel is abruptly decelerated during the dispensing operation, liquid within the capillary channel is momentarily "sheared" or separated from liquid within liquid-supply conduit (abstract).

As seen in the figures, opposed surfaces 108 and 110 of respective elongate members 106a and 106b are concave. Such concave opposed surfaces can be obtained, for example, by forming a slit in a capillary tube. In a second embodiment,

opposed surfaces 108 and 110 are substantially flat. Such flat opposed surfaces can be obtained, for example, by forming a slit in a solid rod (column 3, lines 34-41).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 66-70, 75-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinsky, Moore et al., Feygin as applied to claim 40 above, and further in view of Zaffaroni et al. US 6,121,048.

Martinsky, Moore, nor Feygin disclose the assembly as including a substrate comprising an array of target loci for deposition of sample material.

Zaffaroni et al. disclose an apparatus and method is provided for preparing and using a very large and diverse array of compounds on a substrate having rapidly accessible locations (abstract).

As a synthesis tool, the invention can be used to prepare arrays of diverse polymers. This is accomplished by successively depositing monomers in groups of cells. For example, assume a monomer "A" is to be bound to the substrate in a first group of selected cells. If necessary, all or part of the total array of cells is activated for binding by flowing appropriate reagents over all or part of the substrate, or by depositing the appropriate reagents (with a dispenser) in the selected cells for example. After the dispenser is filled with a reagent containing monomer A, the dispenser and/or the substrate are moved so that the dispenser can deposit a small quantity of monomer A in each of the first group of selected cells. The activated cells are in fluid contact with the dispensed material, thereby binding monomer A on the substrate directly or indirectly (via a linker) (claim 78) in the first selected cells (column 8, lines 15-30).

A collection of peptides or other bio-active compounds can be assayed for activity against one or more receptors. By quickly identifying materials having a strong affinity for the receptor of interest, researchers may discover potential new drugs. In

other embodiments, the arrays produced by the present invention can be used to diagnose, measure, and/or monitor specific conditions in organisms. Specific binding patterns on premade arrays can be expected to accurately identify specific pathogens or other factors present in the sera of a patient. In still other embodiments, the present invention can be used to monitor the quality of pharmaceuticals or other materials, particularly biomolecules produced by, for example, fermentation processes. In such uses, very specific patterns or "fingerprints" on a very large array will correlate with the purity of the compound of interest. Subtle or not so subtle changes in the preparation containing the compound of interest will show up as variations in a baseline binding pattern of the array (column 8, lines 47-67).

The reactant solutions in the individual cells must often be prevented from moving to adjacent cells. This may be ensured by providing an appropriate barrier between the various cells (array of target loci; claims 66-67, 75-77) of the substrate. For example, a hydrophobic material can be used to coat the region surrounding the individual cells. Such materials prevent aqueous (and certain other polar) solutions from moving to adjacent cells. Of course, when non-aqueous or nonpolar solvents are employed, different surface coatings will be required. By choosing appropriate materials (substrates, hydrophobic coatings, and reactant solvents), one can control the contact angle of the droplet with respect to the substrate surface. Large contact angles are desired because the area surrounding the cell remains unwetted by the solution within the cell. In one embodiment of the invention, the perimeters of the individual cells of an array formed on a hydrophilic substrate are defined by selectively irradiating a surface

covered with photocleavable hydrophobic protective groups. In the irradiated areas, the protective groups are removed from the substrate to form lipophilic cells (claims 68(column 9, lines 12-31).

In one method, various protecting groups are used to control the chemical composition of the surface. For example, a mono-layer of hydrophobic photoprotecting groups can be coupled to, for example, linker molecules attached to the substrate surface. The surface is then selectively irradiated (or otherwise activated) through a mask to expose those regions where the cells are to be located. This cleaves the protecting groups from the substrate surface, causing the cell regions to be less hydrophobic than the surrounding area. Because hydrophobic materials have lower surface free energies (surface tensions) than water, the solution droplet in the cell beads rather than spreads. Suitable hydrophobic protecting groups for use with the present invention include, but are not limited to, the alkyl silanes (e.g., octadecyl silane).

FIG. 1A shows a droplet 700 after it was deposited by a micropipette on a non-wetting mask 702 above a substrate 704 according to the present invention. The aspect ratio shown (dome height equals one-half the width) was empirically determined to be stable using a non-wetting mask having a two millimeter by two millimeter square area (the cell diameter was 0.2835 millimeter). FIG. 1B illustrates a top view of a high-density droplet array 710. The four cells of the array are shown at 712, 714, 716 and 718. Because the cell array is defined with photolithographic techniques and the hydrophobic mask is on the order of one monolayer thick, the droplets can be packed very closely together (column 11, line 43 – column 12 line 12).

As to claims 78-80, it is disclosed such receptors as proteins and nucleic acids may be investigated by the invention (column 6, line 17 – column 7, line 5)

In one particularly useful embodiment, the electrophoretic pump can be used to produce an array containing various fractions of an unknown reactant solution. For example, an extract from a biological material, such as a leaf or cell culture, might contain various unknown materials, including receptors, ligands, alkaloids, nucleic acids, and even biological cells, some of which may have a desired activity (claims 78-80; column 17, lines 28-34).

It would have been obvious to one of ordinary skill in the art at the time of the invention to recognize the dispensers of Martinsky, Moore, or Feygin maybe used or combined with a substrate as taught by Zaffaroni et al. to bind specific target molecules in order to identify them and provide diagnoses for patients.

14. Claims 71-72, and 74 rejected under 35 U.S.C. 103(a) as being unpatentable over Martinsky, Moore et al., or Feygin in view of Zaffaroni et al. as applied to claim 66 above, and further in view of Dahm et al. US 6,399,394.

Martinsky, Moore et al., or Feygin in view of Zaffaroni et al. do not specify the characteristics (contact angle) of the materials which the substrate is comprised.

Dahm et al. discloses a method of testing multiple fluid samples with multiple biopolymer arrays. A cover is assembled to a contiguous substrate carrying on a first side, multiple arrays each with multiple regions of biopolymers linked to the substrate.

The substrates may be fabricated from any of a variety of materials. In certain embodiments, such as for example where production of binding pair arrays for use in

research and related applications is desired, the materials from which the substrate may be fabricated should ideally exhibit a low level of non-specific binding during hybridization events. In many situations, it will also be preferable to employ a material that is transparent to visible and/or UV light. For flexible substrates, materials of interest include: nylon, both modified and unmodified, nitrocellulose, polypropylene, and the like, where a nylon membrane, as well as derivatives thereof, may be particularly useful in this embodiment. For rigid substrates, specific materials of interest include: glass; fused silica, silicon, plastics (for example, polytetrafluoroethylene, polypropylene, polystyrene, polycarbonate, and blends thereof, and the like); metals (for example, gold, platinum, and the like).

The substrate surface onto which the polynucleotide compositions or other moieties are deposited may be smooth or substantially planar, or have irregularities, such as depressions or elevations. The surface may be modified with one or more different layers of compounds that serve to modify the properties of the surface in a desirable manner.

The materials of the substrate are the same as claimed by applicant as such the contact angles are inherently the same.

It would have been obvious to one of ordinary skill in the art to further modify the modified assembly of Martinsky, Moore et al., or Feygin to incorporate a substrate comprised of silicon and polytetrafluoroethylene in order to allow for the transparent substrate to be submitted to optical screening.

Allowable Subject Matter

15. Claim 73 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

16. The following is a statement of reasons for the indication of allowable subject matter: The prior art of record does not teach nor fairly suggest a pin tool, wherein the first material is dimethyldichlorosilane (DMDCS).

Conclusion

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Overbeck, James W. et al.; Rose, Don et al.; Hasan, Leila et al.; Ito, Seiichiro et al.; Tseng, Fan-Gang et al.; Dahm, SueAnn C. et al.; Virtanen, Jorma; Stuelpnagel, John R. et al.; Kowallis, Reid Burton; Wolk, Jeffrey A. et al.; Rampal; Jang B. et al.; Pelrine; Ronald E. et al.; Ito; Garyantes; Tina; Kowallis; Reid Burton; Feygin; Ilya; and Roach; David J. et al. disclose dispensing devices and receiving substrates.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is 571-272-1258. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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